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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/848,271	05/04/2001	Steven M. Ruben	PF526	7683

22195 7590 06/18/2003

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EXAMINER	
O HARA, EILEEN B	

ART UNIT	PAPER NUMBER
1646	15

DATE MAILED: 06/18/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/848,271	RUBEN ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 33-43 are pending in the instant application. Claims 24 and 26 have been canceled as requested by Applicant in Paper Number 14, filed March 17, 2003.

Objection to Specification and Claims

2.1 The objection to the specification is withdrawn in view of Applicants' amendment.

2.2 The objection claim 26 is withdrawn in view of Applicants' amendment.

Withdrawn Rejections

3. Any rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Claim Rejections - 35 USC § 101 and § 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 33-43 remain rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility, for reasons of record in the previous Office Action, Paper No. 13, at pages 3-5, and below.

Applicants traverse the rejection and assert that a rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features of characteristics of the invention, or statements made by the applicant in the written description of the invention, and that in addition, an applicant need only make one credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. Applicants further assert that finding a lack

of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed and moreover, that the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt the truth of the statement of utility, and that the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the in the art, and that the Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. Applicants contend that the provision of a number of specific utilities in the specification is proper, and that the Examiner's apparent determination that an asserted utility is not specific or substantial simply because it is not the sole assertion of utility is improper, and furthermore, that although Examiner did not explicitly raise the issue of credibility, Applicants assert that the asserted utility is also credible. Applicants point out that expression levels of Neutrokine-alpha have been shown to be elevated in Sjogren's disease, and submit the publications of Groom et al. and Mariette et al., which teach that patients with Sjogren's Syndrome have elevated levels of Neutrokine-alpha (BlyS or BAFF).

Applicants' arguments have been fully considered but are not deemed persuasive. First, Applicants' contentin that the determination that the utility was not specific and substantial because it is not the sole assertion of utility is not correct. Applicants can assert any number of utilities; however there at least one asserted utility must be specific and substantial, and this had not been shown in the present case. The publications of Groom et al. and Mariette et al. support the assertion that the TR18 receptor of the instant invention could be used diagnostically to detect Sjogren's disease. However, at the time of filing of the instant application, the prior art

did not teach that patients with Sjogren's Syndrome have elevated levels of Neutrokine-alpha. A search of the literature revealed that the first report that Neutrokine-alpha levels were elevated in patients with Sjogren's Syndrome was in January, 2002 (Groom et al. reference). The instant specification also did not teach that Neutrokine-alpha levels were elevated in patients with Sjogren's Syndrome, and merely stated that the TR18 receptor could be used for diagnosis, prognosis or treatment of various immune system-related disorders, and then lists an extensive number of diseases or disorders, one of which was Sjogren's Syndrome (page 132, lines 21-27, page 169, line 9 to page 173, line 23). Because the specification has not provided any evidence that neutrokine-α or APRIL are differentially expressed in Sjogren's disease (or any asserted disease listed), and presents an extensive list of diseases or disorders that may be diagnosed using the TR18 polypeptides, the method of detecting Sjogren's disease is not a specific and substantial utility. At the time of filing of the instant application, there was no nexus between differential expression of neutrokine-α or APRIL and Sjogren's disease, so that one of ordinary skill in the art would not have been able to use the methods. Utility has to be established as of when the invention was made, and all Applicants had was an invitation to experiment. Determining whether levels are elevated or reduced and what is normal is part of the invention. The proposed use of the claimed invention is simply a starting point for further research and investigation into practical uses of the protein. This further experimentation is a useful in basic research, but does not constitute a specific, substantial or well-established utility. Because there is no specific and substantial utility asserted, credibility cannot be assessed. For these reasons and those of record in the previous Office Actions, the rejection under 35 USC § 101 is maintained.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 33-43 also remain rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if the specification were enabling of using the polypeptide of SEQ ID NO: 2 to detect Sjogren's disease, enablement would not be found commensurate in scope with the claims. Claims 41-43 encompass a method of detecting Sjogren's disease comprising contacting an isolated antigenic epitope of the amino acid sequence of SEQ ID NO: 2 with a biological sample. Applicants have amended claim 41 to replace "a polypeptide comprising an antigenic epitope" with "an antigenic epitope" of SEQ ID NO: 2. The specification defines an antigenic epitope on page 55 as containing a sequence of at least 4 amino acids, so that the claims now encompass a method of contacting a biological sample with a peptide fragment as small as 4 amino acids. The basis of the method is the binding of the receptor of SEQ ID NO: 2 to neutrokine-alpha in the biological sample, and such binding would require at least a significant portion of the extracellular domain of the protein of SEQ ID NO: 2. One of ordinary skill in the art would not expect that a peptide fragment of 4 amino acids (or the other peptides of claim 42) would bind to neutrokine-alpha with any type of specificity. Receptor-ligand binding is very specific, and relies on the three dimensional structures of the proteins, as evidenced by Locksley et al., Cell, Vol. 104, pages 487-501 (see entire article, and especially Figure 1). Therefore, even if the specification were enabling for detecting Sjogren's

disease with the polypeptide of SEQ ID NO: 2, it would not be enabling for such a method with a small peptide fragment of SEQ ID NO: 2.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 33-43 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 33-43 are indefinite because claims 33, 36, 39 and 41 are incomplete method claims, and are not written with the different methods steps clearly recited. Although Applicants have amended the claims to include the limitation "wherein altered binding of neutrokine-α indicates the presence of Sjogren's disease" or "wherein altered antibody binding indicates the presence of Sjogren's disease", the claims are still indefinite. A method of contacting a biological sample from a patient with Sjogren's disease would not result in altered binding – it would result in binding of more of the polypeptide of SEQ ID NO: 2 or more of the antibody. Additionally, there are no control steps, such as comparing the degree of binding with a biological sample from normal individual.

It is believed that all pertinent arguments have been answered.

Conclusion

7. No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

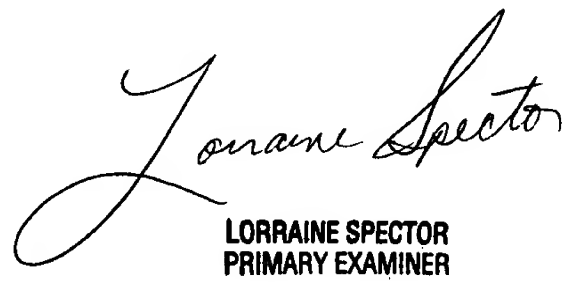
Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



LORRAINE SPECTOR
PRIMARY EXAMINER